

**WHAT IS CLAIMED IS:**

1. A method of quantitating IL-1 $\beta$  in a bone marrow preparation comprising;  
2. a) culturing stromal cells with said bone marrow preparation;  
3. b) determining the amount of IL-6 produced by said stromal cell culture; and  
4. c) correlating the amount of IL-6 produced to the IL-1 $\beta$  concentration in said  
5. bone marrow preparation by comparison to a standard curve prepared by  
6. measuring IL-6 produced by stromal cells contacted with known  
7. concentrations of IL-1 $\beta$ .

*Subj C1*

2. The method of claim 1, wherein said bone marrow preparation is from a patient suffering from multiple myeloma (MM) or a multiple myeloma-related plasmacell proliferative disorder.

3. A method of detecting multiple myeloma (MM) in an individual comprising:

a) culturing stromal cells with a bone marrow preparation from said individual; and

b) determining the amount of IL-6 produced by said stromal cell culture, wherein an elevated level of IL-6 is indicative of MM.

2 4. A method of identifying a patient with a multiple myeloma-related plasmaproliferative disorder likely to progress to active multiple myeloma (MM) comprising:

- a) culturing stromal cells with a bone marrow preparation from said patient; and
- b) determining the amount of IL-6 produced by said stromal cell culture, wherein an elevated level of IL-6 is indicative of a likelihood said patient will progress to active MM.

5. The method of claim 4, wherein said multiple myeloma-related plasmaloproliferative disorder is monoclonal gammopathy of undetermined significance (MGUS).

25           6.       The method of claim 4, wherein said multiple myeloma-related  
26       plasmabrolytic disorder is smoldering multiple myeloma (SMM).

1 7. (c) The method of claims 3 or 4, wherein an elevated level of IL-6 is a  
2 concentration of IL-6 greater than that produced by stromal cells incubated with 1 pg/ml of  
3 recombinant IL-1 $\beta$ .

8. The method of any one of claims 1-7, wherein said bone marrow preparation is selected from the group consisting of a fresh supernatant from cultured bone marrow cells, a previously frozen supernatant from cultured bone marrow cells and a mononuclear cell preparation purified from bone marrow.

9. The method of any one of claims 1-7, wherein an inhibitor of IL-1 $\beta$  is added to the stromal cell culture of step a).

10. The method of claim 9, wherein said inhibitor of IL-1 $\beta$  is selected from the group consisting of an anti-IL $\beta$  antibody, a soluble IL-1 receptor (sIL-1R) type I, a sIL-1R type II, an interleukin-1 receptor antagonist (IL-1ra) and an IL-1 TRAP.

11. A method of identifying a patient with a multiple myeloma-related plasmaproliferative disorder likely to progress to active multiple myeloma (MM) comprising:

- a) culturing a bone marrow preparation from said patient with a T-cell line that produces IL-2 in response to IL-1 $\beta$ ;
- b) determining the amount of IL-2 produced by said T-cell line; and
- c) identifying said patient as likely to progress to MM if said amount of IL-2 is elevated.

12. The method of claim 11, wherein said multiple myeloma-related plasmaproliferative disorder is monoclonal gammopathy of undetermined significance (MGUS).

23 13. The method of claim 11, wherein said multiple myeloma-related  
24 plasmabproliferative disorder is smoldering multiple myeloma (SMM).

1 14. The method of claim 11, wherein said T-cell line is selected from the group  
2 consisting of EL4.6.1, LBRM 33 and primary cultures of thymocytes.

Sub C 4  
3 15. A method of monitoring the effectiveness of the treatment of a patient  
4 with multiple myeloma (MM) comprising:  
5 a) culturing stromal cells with a bone marrow preparation from said patient after  
6 the initiation of treatment;  
7 b) determining the amount of IL-6 produced by said stromal cell culture; and  
8 c) comparing said amount of IL-6 with a known standard or a patient determined  
9 standard.

10 16. A method of treating a patient with multiple myeloma (MM) comprising:  
11 a) identifying a patient with MM; and  
12 b) administering an inhibitor of interleukin-1J (IL-1J) to said patient.

13 17. A method of inhibiting interleukin-6 (IL-6) production by bone marrow  
14 stromal cells in a patient suffering from multiple myeloma (MM) or a multiple myeloma-  
15 related plamaproliferative disorder comprising administering an inhibitor of interleukin-1 $\beta$   
16 (IL-1 $\beta$ ) to said patient in an amount effective to inhibit the production of IL-6 by said bone  
17 marrow stromal cells.

18 18. A method of inhibiting interleukin-6 induced myeloma cell proliferation in a  
19 patient suffering from multiple myeloma (MM) or a multiple myeloma-related  
20 plamaproliferative disorder comprising administering an inhibitor of interleukin-1 $\beta$  (IL-1 $\beta$ )  
21 to said patient in an amount sufficient to inhibit myeloma cell proliferation.

22 19. The method of either of claim 17 or claim 18, wherein said multiple myeloma-  
23 related plamaproliferative disorder is selected from the group consisting of monoclonal  
24 gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM)  
25 and indolent multiple myeloma (IMM).

1        20. A method of inhibiting the progression from monoclonal gammopathy of  
2 undetermined significance (MGUS) to multiple myeloma (MM) in a patient suffering from  
3 MGUS comprising administering an inhibitor of interleukin-1 $\beta$  (IL-1 $\beta$ ) to said patient.

4        21. A method of inhibiting the progression from smoldering multiple myeloma  
5 (SMM) to multiple myeloma (MM) in a patient suffering from SMM comprising  
6 administering an inhibitor of interleukin-1 $\beta$  (IL-1 $\beta$ ) to said patient.

7        22. The method of any one of claims 17-21, wherein said inhibitor of IL-1 $\beta$  is  
8 selected from the group consisting of an anti-IL $\beta$  antibody, a soluble IL-1 receptor (sIL-1R)  
9 type I, a sIL-1R type II, an interleukin-1 receptor antagonist (IL-1ra) and an IL-1 TRAP.

10        23. A kit comprising:

- 11        a) an inhibitor of bioactive IL-1 $\beta$ ;
- 12        b) a negative control for the inhibitor of bioactive IL-1 $\beta$ ; and
- 13        c) a positive control for bioactive IL-1 $\beta$ .

14        24. The kit of claim 23, wherein the inhibitor of bioactive IL-1 $\beta$  is selected from  
15 the group consisting of an anti-IL $\beta$  antibody, a soluble IL-1 receptor (sIL-1R) type I, a sIL-  
16 type II, an interleukin-1 receptor antagonist (IL-1ra) and an IL-1 TRAP.

17        25. The kit of claim 23, wherein said positive control for bioactive IL-1 $\beta$  is  
18 recombinant IL-1 $\beta$ .

19        26. The kit of claim 23, further comprising a label or package insert indicating  
20 that said positive control for bioactive IL-1 $\beta$  is used to prepare a standard curve of IL-6  
21 produced by stromal cells contacted with known concentrations of bioactive IL-1 $\beta$ .

22        27. The kit of claim 23 further comprising bone marrow stromal cells.